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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,039	02/08/2001	Gregory S. Friedrichs	AM100143	4428

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WYETH
PATENT LAW GROUP
FIVE GIRALDA FARMS
MADISON, NJ 07940

EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/779,039	FRIEDRICHS ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- *The MAILING DATE of this communication appears n the cover sheet with the c rrespondence address* --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *6,12 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11 and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *8* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Formal Matters

Claims 1-17 are pending. Claims 6, 12, 17 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-5, 7-11, 13-16 are under consideration.

Response to Arguments

Applicant's arguments filed in Paper No. 7, 3/21/2003 have been fully considered but they are persuasive in part.

The rejection of claims 1-5, 7, 9-11, 13-16 under 35 U.S.C. 102(b) as being anticipated by Deswal et al. (1999) has been withdrawn based on Applicants claim for priority to U.S. Provisional Application 60/240,935, as set forth on the corrected application datasheet.

New and remaining issues are set forth below

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 7, 9-11, 13-16 are rejected under 35 U.S.C. 102(a) as being anticipated by Deswal et al. (1999).

Deswal et al. teaches the selection of patients in need of therapy for an ischemic event in a mammal, and the administration of a TNF antagonist to treat said mammal. In this study Eighteen NYHA class III heart failure patients were randomized into a double-blind dose-escalation study to examine the safety and potential efficacy of etanercept, a specific TNF

antagonist (Enbrel) (Deswal at 3224). Of the patients enrolled in the study, 4 had ischemic heart disease (Ibid. at 3225, Table I), thus claims 1, 2 are anticipated. Etanercept contains 2 molecules of the extracellular domain of sTNFR2 linked to the Fc portion of the IgG1 molecule (Ibid. at 3225), thus claims 3-5 are anticipated. Myocardial infarction is an ischemic event, thus claims 13-16 are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-11, 13-16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Deswal et al. (1999) in view of Ferrari et al. (1999), for reasons of record set forth in Paper No. 6, 10/21/2002.

Deswal et al. teaches the selection of patients in need of therapy for an ischemic event in a mammal, and the administration of a TNF antagonist to treat said mammal. In this study Eighteen NYHA class III heart failure patients were randomized into a double-blind dose-escalation study to examine the safety and potential efficacy of etanercept, a specific TNF antagonist (Enbrel) (Deswal at 3224). Of the patients enrolled in the study, 4 had ischemic heart disease (Ibid. at 3225, Table I). Etanercept contains 2 molecules of the extracellular domain of sTNFR2 linked to the Fc portion of the IgG1 molecule (Ibid. at 3225). Myocardial infarction is an ischemic event. Deswal et al. does not teach a method of inhibiting reperfusion injury in a mammal in need of treatment thereof with a TNF antagonist. Ferrari et al. teaches that there is increasing evidence that cytokines in general and tumour necrosis factor (TNF) in particular play an important role in cardiovascular disease. Increased levels of TNF have been implicated in the pathophysiology of ischemia-reperfusion injury, myocarditis, cardiac allograft and also in the progression of congestive heart failure (Ferrari at 99). Thus, it would have been obvious to one of skill in the art at the time the invention was made to practice a method of treating mammals in need of treatment for an ischemic event, myocardial infarction or reperfusion injury, with a TNF antagonist such as etanercept. The motivation is provided in Ferrari et al. who teaches that the extent of the increase in TNF levels is related to the severity of the syndrome, and that the cytokines contribute to the severity and progression of congestive heart failure (Ibid at 99), and that treatment with anticytokine therapy is safe (Ibid. at 102).

Applicant argues that the Ferrari reference is a general reference which states the hypothesis that TNF may be involved in the progression of congestive heart failure, and that anti-TNF strategies may be considered for therapeutic strategies, while Deswal was reporting the

treatment of patients in the final stages of a chronic heart disease, and that the references do not teach the administration of a TNF-antagonist following an ischemic event as claimed. However, the Deswal reference teaches the administration of a TNF antagonist, etanercept to patients afflicted with an ischemic condition, see Deswal at 3225, Table I, which indicates that 15 the 18 total patients had ischemic heart disease. The Ferrai reference teaches that TNF has been shown to be increased in the myocardium after experimental ischemia and reperfusion, and that the extent of the increase is related to the severity of the syndrome. The skilled artisan would thus be motivated to practice a method of administration of etanercept, a TNF antagonist, to a mammal with a reperfusion injury because of the effectiveness in treating ischemic injury as shown in Deswal et al. with the teaching in Ferrari et al. that the extent of the increase in TNF levels is related to the severity of the syndrome, and that the cytokines contribute to the severity and progression of congestive heart failure, and that treatment with anticytokine therapy is safe. In addition, the combination of Ferrari and Deswal would give the skilled artisan a reasonable expectation of success, given that the Ferrari reference teaches that there is a role for TNF in congestive heart failure, and also teaches that anti-TNF strategies may be considered for therapeutic strategies, when combined with the teaching in Deswal that anti-TNF therapeutic strategies are efficacious in patients with heart failure as a result of an ischemic event. Thus, the combination of Ferrari and Deswal give a reasonable expectation of success because of the shown efficacy of the anti-TNF therapy when combined with the teaching of the role of TNF in congestive heart failure as a result of an ischemic event.

Conclusion

No claim is allowed.

Applicant's amendment, which perfected the priority claim, necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

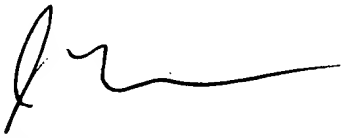
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
August 12, 2003